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Quantitative sensory testing of temperature, pain, and touch in adults with Down syndrome



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ABSTRACT

The spinothalamic pathway mediates sensations of temperature, pain, and touch. These functions seem impaired in children with Down syndrome (DS), but have not been extensively examined in adults. The objective of the present study was to compare the spinothalamic-mediated sensory functions between adults with DS and adults from the general population and to examine in the DS group the relationship between the sensory functions and level of intellectual functioning. Quantitative sensory testing (QST) was performed in 188 adults with DS (mean age 37.5 years) and 142 age-matched control participants (median age 40.5 years). Temperature, pain, and touch were evaluated with tests for cold–warm discrimination, sharp–dull discrimination (pinprick), and tactile threshold, respectively. Level of intellectual functioning was estimated with the Social Functioning Scale for Intellectual Disability (intellectual disability level) and the Wechsler Preschool and Primary Scale of Intelligence – Revised (intelligence level). Overall, the difference in spinothalamic-mediated sensory functions between the DS and control groups was not statistically significant. However, DS participants with a lower intelligence level had a statistically significant lower performance on the sharp–dull discrimination test than DS participants with higher intelligence level (adjusted $p = .006$) and control participants (adjusted $p = .017$). It was concluded that intellectual functioning level is an important factor to take into account for the assessment of spinothalamic-mediated sensory functioning in adults with DS: a lower level could coincide with impaired sensory functioning, but could also hamper QST assessment.

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Individuals with Down syndrome (DS) have a higher prevalence of certain physical conditions that may cause pain, such as neck conditions and hip dislocation (Bull, 2011; Charleton, Dennis, & Marder, 2010; Smith, 2001). However, individuals with DS show a weak tendency to complain of pain (Smith, 2001) and seem slower in detecting pain (Aguilar Cordero, Mur Villar, & García García, 2015; Defrin, Pick, Peretz, & Carmeli, 2004; Hennequin, Morin, & Feine, 2000). Adequate pain management requires a better understanding of how individuals with DS experience pain. This could be supported by insight into the functioning of the somatosensory system, which transmits somatosensory information from peripheral receptors via the spinal cord and brain stem primarily to the thalamus and somatosensory cortex (Almeida, Roizenblatt, & Tufik, 2004; Kaas, Jain, & Qi, 2002). The somatosensory cortex plays a major role in the processing of pain (Kanda et al., 2000). Spinothalamic-mediated sensory functions are the abilities to detect sensations of pain, temperature (innocuous and noxious), and crude touch (Almeida et al., 2004; Fitzgerald, Gruener, & Mtui, 2007).

Techniques to map brain activity, such as electroencephalography (Chen & Fang, 2005; Cruccu et al., 2008) and functional magnetic resonance imaging (Gröschel et al., 2013), can be used to examine the functioning of the general somatosensory system. However, these methods could be stressful (Downie & Marshall, 2007) and are not always available in health care facilities for individuals with intellectual disabilities. Quantitative sensory testing (QST) facilitates assessment of nervous system functioning by using standardized tests for thresholds and stimulus-response functions (Arendt-Nielsen & Yarnitsky, 2009). The use of QST instruments to assess temperature discrimination, sharp–dull discrimination, and tactile threshold was found to be feasible in 85–88% of children with DS (Valkenburg, Van Dijk, & Tibboel, 2015).

Several studies have been conducted on spinothalamic-mediated sensory functions in individuals with DS. Compared to control participants, children and adults with DS had more difficulty in localizing cold stimuli and had a longer reaction time (RT) between the application of cold stimuli and the verbal indication of pain, suggesting a high cold-pain threshold (Hennequin et al., 2000). A higher cold-pain threshold was however not confirmed by quantitative sensory test results in children with DS (Valkenburg et al., 2015). When using RT-dependent measurements, the heat-pain threshold was comparable to control participants in adults with DS (Defrin et al., 2004) but was higher in children with DS (Valkenburg et al., 2015). In addition, the detection thresholds for cold and warmth were higher in children with DS than control participants, but this group difference disappeared when using an RT-free method (Valkenburg et al., 2015). Fewer children with DS than control participants were able to discriminate all stimuli between cold and warmth, to discriminate all stimuli between sharp and dull, and to detect the lowest possible tactile threshold of .026 g, with statistically significant group differences (Valkenburg et al., 2015).

The question arises whether spinothalamic-mediated sensory functions are also impaired in adults with DS. It is important to examine these functions over the entire life span of individuals with DS, because additional painful conditions emerge in adulthood, such as early onset of cervical arthritis (Ali, Al-Bustan, Al-Busairi, Al-Mulla, & Esbaita, 2006), and the functioning of the somatosensory system may decrease with aging (Shaffer & Harrison, 2007). Therefore, the next step is to examine the functions of the same somatosensory pathway (i.e., spinothalamic-mediated sensory functions of temperature, pain, and touch) in a large sample of adults with DS. Because individuals with Down syndrome form a heterogeneous group, with a mild to severe level of intellectual disability (Patterson, 2009) and an IQ ranging from 30 to 70 (Chapman & Hesketh, 2000), the level of intellectual functioning needs to be taken into account. The research questions of the present explorative study were: (1) are spinothalamic-mediated sensory functions (temperature discrimination, sharp–dull discrimination, and tactile threshold) in adults with DS different from general population control participants? and (2) are spinothalamic-mediated sensory functions in adults with DS related to level of intellectual functioning?

1. Materials and methods

1.1. Study design and ethical approval

A cross-sectional study was performed, including both between-group and within-group analyses, in 188 adults with DS and in 142 adults from the general population. Approval was obtained by the Medical Ethical Committee of VU University Medical Center in Amsterdam (NL33540.029.11).

1.2. Participants

1.2.1. Down syndrome group

Adults with DS were recruited from 15 care centers for individuals with intellectual disabilities (with permission from the Management Board) and through the Dutch Down Syndrome Foundation. Inclusion criteria were: 18 years of age or older, speaking and understanding Dutch, and the capability to verbally answer simple questions (e.g., “What is your name?”). Exclusion criteria were neurological disorders (e.g., cerebrovascular accidents or tumors), severe visual impairments or hearing loss, and the use of antipsychotics, anticonvulsants, or antidepressants. If there was doubt regarding participants’ capacity to provide informed consent, consent was also required from parents or guardians. In case of any sign of resistance, assessments were curtailed. Participants were only included in the analyses if they had completed all three spinothalamic-mediated sensory tests, resulting in a decrease from 232 to 188 participants with DS. Reasons for failing to complete a spinothalamic-mediated sensory test are described in Table 1.

Table 1

Reasons for failing to complete the spinothalamic-mediated sensory function tests by 44 participants with Down syndrome.

Reason for failing to complete test	Rolltemp: <i>n</i>	Neuropen: <i>n</i>	Von Frey: <i>n</i>
Instrument not available	7	8	7
Unknown	2	8	3
Lack of comprehension of test instructions	5	7	8
Fear, anxiety, or phobia (phobia of needles)	0	7	2
Sharp stimulus is experienced as too painful to continue	0	3	0
Unable or unwilling to close the eyes	3	4	3
Refusing to cooperate (unspecified)	0	2	0
Total (>44 because 1 participant could fail > 1 test)	17	39	23
Total with available tests (<i>n</i> = 36 of 224 = 16%)	10 (4.5%)	31 (14%)	16 (7%)

Note: Instrument available = in protocol and not left at university: *n* = 44–8, because QST instruments were not yet included in the protocol for 7 participants (they were part of the pilot study in which more simple instruments for spinothalamic-mediated sensory functions were used of which data could not be included in the current paper) and the Neuropen was left at the university in one participant. The total number of participants in whom the tests were applied were therefore 232–8 = 224. Percentages per test in the lowest row represent total% of participants failing on the test of the total group participants in whom the tests were available (*n* = 224).

In the subgroup of participants who were excluded (*n* = 44), statistically significant results were revealed for a higher average age ($t(230) = 2.83$, $p = .005$, $M_{\text{excluded}} = 42.7$, $M_{\text{included}} = 37.5$, $r = .18$), a lower average intelligence level ($t(199) = -2.55$, $p = .012$, $M_{\text{excluded}} = 4.4$, $M_{\text{included}} = 5.1$, $r = .18$), more participants with a severe level of intellectual disability ($\chi^2(2) = 7.72$, $p = .021$, $\Phi = .18$, 21% versus 7% severe level), and more participants who used analgesics (Fisher's Exact test, $p = .001$, $\Phi = -.25$, 16% versus 2% users) compared to the subgroup of participants who were included (*n* = 188). No statistically significant associations were found between 'subgroup' on the one hand and gender ($\chi^2(1) = <.01$, $p = .96$, $\Phi = <-.01$), living situation ($\chi^2(1) = 2.66$, $p = .10$, $\Phi = .11$), possible dementia indication (Fisher's Exact test, $p = .68$, $\Phi = .08$), possible pain/discomfort ($\chi^2(1) = 3.55$, $p = .06$, $\Phi = -.12$), and possible neuropathic pain (Fisher's Exact test, $p = 1.00$, $\Phi = .02$) on the other.

1.2.2. Control group

General practitioners (GPs) who had signed a letter of intent approached potential participants from their general medical practice according to inclusion and exclusion criteria. In addition, the researchers asked their family members and acquaintances with varied age, gender, and level of education to participate without informing them about the hypotheses of the study. Following informed consent, the testing took place. Inclusion criteria for the control group were: 18 years of age or older and speaking and understanding Dutch. Exclusion criteria were: cognitive impairment, severe visual impairments or hearing loss, current depressive symptoms or an anxiety disorder, use of anticonvulsants, antidepressants or antipsychotics, and excessive alcohol use. The exclusion criterion of cognitive impairment was checked by assessing the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975). No participants scored below the cut-off of 24 (Tombaugh & McIntyre, 1992), therefore no participants were excluded.

Because the average age of the control group ($M = 43.3$, $SD = 16.8$) was higher than that of the DS group ($M = 37.5$, $SD = 11.3$; $t(270) = 3.75$, $p < .001$, $r = .22$), control group participants aged older than 65 years were excluded. This matching of groups on age resulted in an age range of 18–65 years in both groups and a decrease from 160 to 142 participants in the control group.

1.3. Material for background variables

Intelligence level in DS participants was estimated by using the subtests Block Design and Vocabulary of the Wechsler Preschool and Primary Scale of Intelligence – Revised version (WPPSI-R; Wechsler, 1989). The dyad of these two subtests has a high excellent reliability ($r = .87$) and a high correlation ($r = .83$) with the Full IQ of the WPPSI-R (Sattler, 2001). The WPPSI-R, standardized for children aged 3–6 years, has been used in adults with DS before (Raz et al., 1995). The average mental age in adults with DS is about 5 years (Carr, 1994, 2000) and the use of adult intelligence tests would lead to a floor effect (Raz et al., 1995). Participant had to construct patterns with blocks within a limited time and describe verbally the meaning of words. Afterwards, the age equivalents in years and months (2;01–10;10) corresponding to the raw scores of both subtests were retrieved from a manual about psychodiagnostic assessment in individuals with intellectual disabilities (Kraijer & Plas, 2006) to calculate the average age equivalent (i.e., mental age).

Intellectual disability level was estimated by using the Social Functioning Scale for Intellectual Disability (SRZ or SRZ-P; Kraijer, Kema, & De Bildt, 2004; Kraijer & Kema, 2004). The SRZ and SRZ-P assess social and cognitive abilities and activities of daily living, in which the SRZ-P correspond to a higher level of functioning than the SRZ. The questionnaires have a good reliability and validity (Egberink, Janssen, & Vermeulen, 2014a, 2014b). The SRZ correlates highly with the Vineland Adaptive Behavior Scales (De Bildt, Kraijer, Sytema, & Minderaa, 2005). The caregiver chose whether the SRZ or SRZ-P was more appropriate for the participant's level of functioning (which is important for assessment of possible dementia, as described later). Each total score corresponds to a standardized score by using the population norms of the manual and a standardized score corresponds to a level of intellectual disability by using the "Manual Psychodiagnostics and Limited Ability" (Kraijer &

Plas, 2006). To use only one variable for intellectual disability level, participants of whom only the SRZ-P was available were identified as having a mild level of intellectual disability according to the SRZ.

Participants with DS aged 40 years and older were screened for the possible presence of dementia, defined as a significantly decrease in functioning over time as measured with the SRZ or SRZ-P and the Dementia Questionnaire for Intellectual Disability (DMR; Evenhuis, Kengen, & Eurlings, 2006). The DMR consist of the subscales short-term memory, long-term memory, orientation, speech, practical skills, mood, activity and interest, and behavioral disturbance. The reliability and validity of the DMR are sufficient (Egberink, Janssen, & Vermeulen, 2014c). The questionnaires were completed after the test session and scores of at least six months earlier were derived from files of the care centers. When old scores were missing in the file, then the questionnaires were completed at least six months after the test session were used. A possible indication of dementia was considered to be present if the decrease in the total scores of both the SRZ/SRZ-P and the DMR over the two moments in time was statistically significant according to criteria in the manuals. The use of the DMR criteria has a 100% sensitivity and 75% specificity in elderly with DS (Evenhuis, 1996).

In the control group, education level was categorized by means of a Dutch seven-point education system (Verhage, 1964). Intelligence level was estimated by using the short form of the Groninger Intelligence Test II (GIT-2; Luteijn & Barelds, 2004), which contains the subtests synonyms, mental rotation, visual synthesis, mental arithmetic, word analogies, and fluency. IQ was calculated by means of the manual. The IQ-score from the short form correlates highly with that of the total GIT-2 ($r = .94$, Luteijn & Barelds, 2004). The total form has a sufficient reliability and a satisfactory to good validity (Egberink, Janssen, & Vermeulen, 2014d).

Medical files of the control participants and client files of the DS participants were used to obtain medical information. A physical condition was rated as possibly causing pain or discomfort when at least two of three professionals indicated that this could be the case: specialized physicians for individuals with intellectual disabilities (who first reached consensus), a physiotherapist, and a general physician. The following physical conditions were considered to cause possible neuropathic pain/discomfort: cervicobrachialgia, ulnar neuropathy, carpal tunnel syndrome, diabetes, leg pain with unspecified cause, and foot pain with unspecified cause.

1.4. Assessment of spinothalamic-mediated sensory functions

The participants performed the tests with eyes closed. When this was not possible or reliable, then a caregiver held a hand over the participant's eyes or the participant received a blindfold. Stimuli were administered to the volar aspect of the forearm. This site is often used in somatosensory studies (Olausson, Wessberg, & Kakuda, 2000; Scherder, Rommelse, Bröring, Faraone, & Sergeant, 2008) because of the high density of intra-epidermal nerve fibers (Kawakami, Ishihara, & Miharam, 2001). No time limit was used. A priori, explanation was offered with eyes open and the different stimuli were applied once to ascertain that the participant understood the meaning of the tests and to reduce anxiety.

1.4.1. Temperature

For discrimination of innocuous temperatures, the Rolltemp was used (Somedic AB, Hörby, Sweden; see Figs. 1 and 2). The Rolltemp has been mainly used to measure temperature perception in pain patients (e.g., Kalliomäki et al., 2011) and the cold roller (i.e., "Lindblom roller") has been recommended as a simple instrument to assess cold hypoaesthesia or allodynia (Marchettini, Marangoni, Lacerenza, & Formaglio, 2003). As far as we know, the only information about psychometric properties of the Rolltemp is feasibility in 88% of children with DS (Valkenburg et al., 2015).

A cold metal roller (25 °C) and a warm metal roller (40 °C) were placed in a special base unit that sets the temperatures. The rollers were then applied in standardized random order three times to the right forearm (cold–warm–warm) and three times to the left forearm (warm–cold–warm) of the participant. A comparable distance and speed was used each time: the time to move the rollers at the volar aspect of the forearm between the elbow and the wrist. After each stimulus, the researcher asked "What did you feel?". Correct verbal responses, if corresponding to the applied stimulus, were "warm" and "cold". Correct non-verbal responses were pointing to the corresponding roller. A continuous variable was used for the total of correct answers (ranging from 0 to 6), while a dichotomous variable was used for the number of participants who obtained the maximum score of 6 (=1) and those who did not (=0).

1.4.2. Pain

A neuropen (Owen Mumford Ltd, Oxford, United Kingdom; see Figs. 3–5) was used for the pinprick test to assess sharp–dull discrimination. The Neuropen was found to have a high sensitivity and specificity in assessing peripheral neuropathy in diabetic patients (Paisley, Abbott, Schie, & Boulton, 2002) and a feasibility in 85% of children with DS (Valkenburg et al., 2015). The two sides of the Neuropen were applied in standardized random order three times to the right forearm (sharp–dull–sharp) and three to the left forearm (sharp–dull–dull) to test discrimination between touch, i.e. a nylon monofilament, and sharpness, i.e. a little pin called 'Neurotip'. The monofilament was pressed on the skin surface at a 90° angle until it bowed (10 g) and subsequently held in this position for 2 s. The Neurotip was pressed gently on the skin surface at a 90° angle until the marker was within the 40 g marker zone and subsequently held in this position for 2 s. After each stimulus, the researcher asked "What did you feel?". Correct verbal responses, if corresponding to the applied stimulus, were "sharp" (or "tip") and "soft" (or "hair"). Correct non-verbal responses were pointing to the corresponding side of the Neuropen. A



Fig. 1. Rolltemp with base unit, warm roller (upper) and cold roller (lower). Somedic AB, Hörby, Sweden. Permission for use obtained by Somedic AB.

continuous variable was used for the total of correct answers (ranging from 0 to 6), while a dichotomous variable was used for the number of participants who obtained the maximum score of 6 (=1) and those who did not (=0).

1.4.3. Touch

To assess tactile threshold, nylon monofilaments of increasing diameter were pressed gently on the skin until they bowed (Aesthesiometer, set of 'von Frey hairs' with .026–110 g buckling force, Somedic AB, Hörby, Sweden; see Figs. 6 and 7). Von Frey monofilaments are sensitive in detecting decreased sensibility in healthy adults (Rolke et al., 2006) and are feasible in 88% of children with DS (Valkenburg et al., 2015). An inter-stimulus interval of about 10 s was used. Participants were instructed to verbally indicate ("Yes" or "Now") if they felt something on the forearm. Participants were not asked after each monofilament whether they had felt something, because such a closed question could lead to false positives. Stroking the skin with the hair was avoided. The researcher started with the thinnest monofilament and gradually used larger monofilaments in ascending order until the moment that participants indicated that they felt something. The researcher subsequently applied gradually thinner monofilaments in descending order until participants did not indicate detection anymore. The thinnest monofilament that participants detected was considered to be the tactile threshold. This procedure was then repeated for the other forearm. The average tactile threshold was calculated from the thresholds of the two forearms and ranged from .026 to 110. A dichotomous variable was used for the number of participants who obtained the optimal average tactile threshold of the .026 g monofilament (=1) and those who did not (=0).

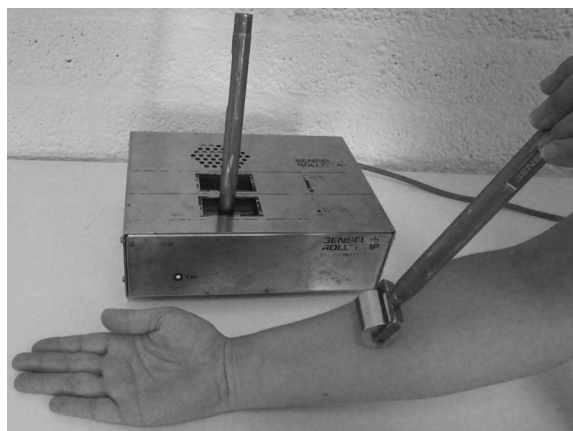


Fig. 2. Use of the rollers on the volar aspect of the forearm (photo made by the researchers).



Fig. 3. Neuropen with location of the Neurotip (1), the spring mechanism to exert a force of 40 g (2), and the monofilament (3). Owen Mumford Ltd, Oxford, United Kingdom.

Permission for use obtained by Owen Mumford Ltd.

1.5. Procedure

DS participants were tested (average time: about 45 min) in a quiet room in their facility for living, work, or daily activities. A caregiver was present as long as it was needed to make the participant feel at ease with the researcher. After the test session, caregivers received the SRZ/SRZ-P and the questionnaire about medication, diabetes, and physical conditions that may cause pain/discomfort or may affect somatosensory function. Participants of the control group were tested (average time: about 60 min) in a quiet room at the general medical practice, at home, or in VU University. They requested their medical file from their general physician and sent it to the university.

1.6. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 21. The level of statistical significance (two-sided) was set at $\alpha = .05$, but was .017 for analyses in which the three sensory functions were included (Bonferroni). Age in the control group and all variables of the spinothalamic-mediated sensory tests were not normally distributed (using skewness and kurtosis). The assumptions for linear regression analysis were violated (Field, 2009). It was impossible to form one component of spinothalamic-mediated sensory function (using Principal Component Analysis and reliability analysis). Estimated intelligence level was missing in 15 (8%) DS participants, because the subtests were not yet included in the study protocol of 10 participants and comprehension of the subtests was insufficient in 5 participants.



Fig. 4. Use of the Neurotip (sharp side) on the volar aspect of the forearm (photo made by the researchers).



Fig. 5. Use of the monofilament (dull side) on the volar aspect of the forearm (photo made by the researchers).



Fig. 6. Von Frey monofilaments of the Aesthesiometer. Somedic AB, Hörby, Sweden. Permission for use obtained by Somedic AB.



Fig. 7. Use of the Von Frey monofilament on the volar aspect of the forearm (photo made by the researchers).

For the first research question, Chi-squared tests were used to associate group with optimal sensory test performance and Mann–Whitney U tests were used to compare groups on sensory test performance. For the second research question, sensory test performance was related to possible dementia indication with Mann–Whitney U tests, was related to intellectual disability level with a Kruskal–Wallis omnibus test, and was related to intelligence level with Spearman correlations. In

addition, a Kruskal–Wallis omnibus test was used to compare lower and higher subgroups of intelligence level (split at the median) with the control group on sensory test performance.

2. Results

2.1. Demographic and medical characteristics of the Down syndrome and control groups

Table 2 shows the characteristics of the groups included participants. No statistically significant results were found for the group difference in age ($U = 11,974.50$, $p = .11$, $r = -.09$) or for the associations between group on the one hand and gender ($X^2(1) = 1.53$, $p = .22$, $\Phi = -.07$), analgesics use (Fisher's Exact test, $p = .34$, $\Phi = -.06$), or possible presence of neuropathic pain/discomfort ($X^2(1) = 1.19$, $p = .28$, $\Phi = -.06$) on the other. However, more participants of the DS group had physical conditions (including neuropathic conditions) that may cause discomfort or pain ($X^2(1) = 5.15$, $p = .023$, $\Phi = .13$). Differences between participants with and without all physical conditions that may cause pain/discomfort were not statistically significant regarding performance on the tests for cold–warm discrimination ($U = 4323.00$, $p = .34$, $r = -.07$), sharp–dull discrimination ($U = 4046.00$, $p = .27$, $r = -.08$), and average tactile threshold ($U = 4009.00$, $p = .22$, $r = -.09$). The same applied for the control group concerning cold–warm discrimination ($U = 2295.00$, $p = .45$, $r = -.06$), sharp–dull discrimination ($U = 2185.50$, $p = .50$, $r = -.06$), and average tactile threshold ($U = 2192.50$, $p = .52$, $r = -.05$). Therefore, no extra variables were taken into account when analyzing subsequently the group differences in spinothalamic-mediated sensory function.

2.2. Comparing spinothalamic-mediated sensory functions between Down syndrome and control groups

In each spinothalamic-mediated sensory test, the majority of the participants in the DS group and the control group achieved the optimal performance: total score of six in the temperature test (98% DS versus 99% control participants), total score of six in the pinprick test (56% DS versus 63% control participants), and detecting the smallest monofilament on both forearms in the tactile threshold test (59% DS versus 66% control participants). The association between group and achieving the optimal performance was not statistically significant (cold–warm discrimination: Fisher's Exact test, $p = .40$, $\Phi = -.06$; sharp–dull discrimination: $X^2(1) = 1.90$, $p = .17$, $\Phi = -.08$; tactile threshold: $X^2(1) = 1.76$, $p = .19$, $\Phi = -.07$). No statistically significant group difference were revealed in the number of correct answers in tests for cold–warm discrimination ($U = 13,157.50$, $p = .29$, $r = -.06$, $Mdn_{DS} = 6.00$, $Mdn_{Control} = 6.00$) and sharp–dull discrimination ($U = 12,085.50$, $p = .096$, $r = -.09$, $Mdn_{DS} = 6.00$, $Mdn_{Control} = 6.00$), nor in the average tactile threshold ($U = 11,893.00$, $p = .052$, $r = -.11$, $Mdn_{DS} = .026$, $Mdn_{Control} = .026$).

2.3. Relating level of intellectual functioning with spinothalamic-mediated sensory functions in the Down syndrome group

The differences between participants with a possible dementia indication ($n = 7$) and those without ($n = 83$) were not statistically significant for cold–warm discrimination ($U = 283.50$, $p = .68$, $r = -.04$), sharp–dull discrimination ($U = 276.50$, $p = .82$, $r = -.02$), and average tactile threshold ($U = 275.50$, $p = .80$, $r = -.03$). The correlation between intellectual disability level (SRZ) and intelligence level (WPPSI-R) was statistically significant ($r_s = -.24$, $p = .001$, $R_s^2 = .06$). The differences between participants of three different levels intellectual disability were not statistically significant for cold–warm discrimination ($H(2) = .32$, $p = .85$, $r = -.06$ to $r = -.01$), sharp–dull discrimination ($H(2) = .39$, $p = .83$, $r = -.04$ to $r = -.02$), and average tactile threshold ($H(2) = 2.03$, $p = .36$, $r = -.12$ to $r < -.01$). No statistically significant association was found between intelligence level and cold–warm discrimination ($r_s = .09$, $p = .27$, $n = 173$, $R_s^2 = .01$) or average tactile threshold ($r_s = -.04$,

Table 2

Demographic and medical characteristics of the Down syndrome group ($N = 188$) and control group ($N = 142$).

Characteristic	Down syndrome group: n	Control group: n
Age in years (range is 18–65 in both groups)	$M = 37.5$ ($SD = 11.3$)	$Mdn = 40.5$ ($IQR = 25$)
Gender: male	100 (53%)	65 (46%)
Living situation: in care center or with family	163 (87%), 25 (13%)	–
Intellectual disability: mild, moderate, severe	50 (27%), 125 (66%), 13 (7%)	–
Estimated intelligence level	$Mdn = 5;05$ ($IQR = 2;0$) year;month	$M = 105.7$ ($SD = 13.3$) IQ
Education: most frequent level (level 6)	–	68 (48%)
Possible indication of dementia	7 (8% of $n = 90 \geq 40$ years)	–
Mini-Mental State Examination score	–	$Mdn = 29.0$ ($IQR = 1$)
Analgesics use	4 (2%)	6 (4%)
All possible pain/discomfort conditions*	91 (48%)	51 (36%)
Possible neuropathic pain/discomfort	6 (3%)	8 (6%)

Note: Estimated intelligence level in Down syndrome group: the average age equivalent (median developmental level of 5 years and 5 months), which was available for 92% of the participants. Level 6 of Verhage's education system: pre-university education, technical college, or higher vocational education. Possible pain/discomfort conditions: number of participants with a possible presence of pain or discomfort (including neuropathic pain) according to reported medical information (physical conditions, complaints, and medication use). Neuropathic pain/discomfort included diabetes.

* Statistically significant difference between groups, $p = .021$.

$p = .64$, $n = 173$, $R_s^2 = < .01$). In contrast, a statistically significant and positive association with sharp–dull discrimination was found ($r_s = .21$, $p = .006$, $n = 173$, $R_s^2 = .04$). This correlation coefficient was small to medium and intelligence level shared 4% of the variance in the ranks of sharp–dull discrimination. ‘Estimated intelligence level’ was therefore split at the median to create a ‘lower subgroup’ (≤ 5.05 , $n = 87$) and a ‘higher subgroup’ (> 5.05 , $n = 86$) for more specific comparisons of the spinothalamic-mediated sensory functions between adults with DS and the control group in Section 2.4.

2.4. Comparing spinothalamic-mediated sensory functions between Down syndrome subgroups and the control group

When using a recoded group variable (0 = control, 1 = lower intelligence level in DS, 2 = higher intelligence level in DS), no statistically significant group difference were found for cold–warm discrimination ($H(2) = 2.75$, $p = .25$) or average tactile threshold ($H(2) = 3.84$, $p = .15$), but it was found for sharp–dull discrimination ($H(2) = 11.18$, $p = .004$). A post hoc test with correction for pairwise comparisons revealed statistically significant differences in sharp–dull discrimination between the control group and DS participants with a lower intelligence level ($H(1) = 30.04$, adjusted $p = .017$, $r = -.18$, $Mdn_{\text{Control}} = 6.00$, $Mdn_{\text{DS lower}} = 5.00$) and between DS participants with a lower and a higher intelligence level ($H(1) = -37.67$, adjusted $p = .006$, $r = -.23$, $Mdn_{\text{DS lower}} = 5.00$, $Mdn_{\text{DS higher}} = 6.00$).

3. Discussion

The aim of the present study was to compare spinothalamic-mediated sensory functions (temperature, pain, and touch) between adults with DS and general population control participants, and to examine in DS the relationship between spinothalamic-mediated sensory functions and level of intellectual functioning. No statistically significant group differences were found in the performance on the tests for temperature discrimination, sharp–dull discrimination, and tactile threshold. Concerning the relationship with intellectual functioning in the DS group, only a statistically significant correlation was found between estimated intelligence level and sharp–dull discrimination. DS participants with a lower intelligence level (mental age 2;07–5;05 years) had a statistically significant lower performance on the sharp–dull discrimination test than DS participants with a higher intelligence level (mental age 5;06–10;03 years) and than the control group.

The results are in contrast to findings of a recent study in which similar QST tests were used in children with DS (Valkenburg et al., 2015). In that study, statistically significantly fewer children with DS than control participants reached the optimal performance (i.e., no error in the discriminative tests and a tactile threshold of .026 g), while no statistically significant group difference in optimal performance was found in the present study. This may indicate an improvement in spinothalamic-mediated sensory functioning over age, although such an age effect has only been found previously for temperature discrimination in healthy children and adolescents (Blankenburg et al., 2010). It is also possible that the use of three instead of five stimuli in the discriminative tests of the present study may have limited the chance to detect sensory dysfunction. The fact that no statistically significant group differences in tactile threshold were revealed in the present study seems to contrast with the previously found impairment in tactile finger discrimination, tactual perception of letters traced on the palm, and tactual object recognition in children with DS (Brandt, 1996). However, such functions of proprioception and discriminative touch are mediated by the dorsal column instead of the spinothalamic pathway (Almeida et al., 2004; Fitzgerald et al., 2007).

Our finding that the difference in sensory test performance between intellectual disability levels (based on SRZ) was not statistically significant is in line with the previous finding that the association between developmental age (based on Vineland Adaptive Behavior Scales) and feasibility of sensory test performance was not statistically significant in children with DS (Valkenburg et al., 2015). These questionnaires both assess adaptive functioning and are highly correlated (De Bildt et al., 2005). It is difficult to explain the statistically significant decreased ability to discriminate sharp and dull in DS participants with a lower estimated intelligence. One explanation might be that a diminished sharp–dull discrimination could be related to disturbed functioning of Aδ fibers (Walk et al., 2009). A lower sensitivity to detect sharp, painful stimuli may add to explanations for the observed weak tendency in individuals with DS to complain about pain (Smith, 2001). Further, the mediodorsal thalamic nucleus is smaller in adults with DS than in control participants (Karlsen, Korbo, Uylings, & Pakkenberg, 2014); this nucleus is crucial in projecting sensory information to the prefrontal cortex (McFarland & Haber, 2002) and is part of the neural pain systems (Scherder, Sergeant, & Swaab, 2003).

However, pain experience is a complex phenomenon (Woolf, 2004). Cognitive ability is also involved: for example, memory retrieval, adaptive learning, and decision making are cognitive–evaluative aspects of pain (Moriarty & Finn, 2014). Performing the sensory tests required participants to comprehend the instructions and to use the proper words in a direct reaction to the sensation (e.g., “sharp” or “tip” and “dull” or “hair”). Although a priori the meaning of the tests was explained extensively and participants were also allowed in the discriminative tests to respond non-verbally by pointing to the stimulus, the difference between the sharp and dull stimuli may have been confusing. The monofilament of 10 g (dull stimulus) was somewhat difficult to bow, resulting in a subtle difference between the dull and sharp sensations. The instructions may have been more difficult to comprehend than the discrimination between warm and cold (Rolltemp) and between no touch and touch (Von Frey hairs). This could implicate that the Neuropen should not be used for adults with DS in a lower intelligence level.

3.1. Limitations

The scores for the level of intellectual disability should be interpreted with caution as the use of the SRZ-P or SRZ appeared incorrect for seven participants according to guidelines in the manuals. Further, the scores for estimated intelligence level should be interpreted with caution as our Dutch translations of 3 of the 12 words on the WPPSI-R Vocabulary test were different from the official forward-backward translations, which may have resulted in a slight over-estimation of the average age-equivalent score. Also, the use of the Block Design and Vocabulary subtests of the Wechsler Adult Intelligence Scale (WAIS-IV; Wechsler, 2012) to estimate IQ in the control group would have been more in line with the use of the WPPSI-R subtests in the DS group.

3.2. Recommendations

There is a need for research on the psychometric properties of the Rolltemp, Neuropen, and Von Frey tests in intellectually disabled individuals, also because the use of these instruments seems more feasible in individuals with DS than the Thermal Sensory Analyzer (Valkenburg et al., 2015). The current findings need to be replicated in a study involving both children and adults with DS to study the relationship between age and spinothalamic-mediated sensory functions. The use of diffusion tensor imaging could provide insight into the relationship between neuronal white matter pathways and intelligence level (Yu et al., 2008), but could also be stressful (Downie & Marshall, 2007). QST can have clinically relevant applications for physicians and physiotherapists to assess sensory abnormalities such as hypoesthesia or allodynia (Arendt-Nielsen & Yarnitsky, 2009; Marchettini et al., 2003) in individuals with intellectual disabilities. However, the lower intelligence level and intellectual disability level in the participants who were excluded show that the tests may not be feasible for each individual. Causes of resistance, such as fear for needles (see Table 1) or the presence of pain, should be examined and tests should never be used against someone's will.

3.3. Conclusion

The results suggest that the abilities of adults with DS to discriminate temperatures, to discriminate sharp and dull, and to detect touch are not impaired compared to adults from the general population. However, adults with DS with a lower intelligence level may have a diminished ability to discriminate sharp from dull. While this is clinically relevant for a better understanding of their pain experience, these individuals could also show resistance to participate or may have difficulties with comprehending test instructions. More research is needed to understand spinothalamic-mediated sensory functions in adults with intellectual disabilities and to learn about the clinical possibilities of QST in this target population.

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